Remarks

This amendment is presented to place this application in condition for examination.

The specification is amended to reference Applicants' parent applications.

In the specification for the application as filed herewith, a change has been affected in TABLE III regarding the "pKi" values for Compounds M and N. This change was effected by amendment in Serial No. 10/385,522 and is proper for the reasons noted when effecting the change. The change was not objected to by the Examiner during prosecution of Serial No. 10/385,522.

Attached hereto is a marked-up version of original page 27 of the specification showing the changes effected.

The claims of the application are amended by cancelling, without prejudice to the subject matter thereof, claims 1 - 8 and inserting in their stead new claim 9 which is directed to the subject matter to be prosecuted in the present application. Support for the newly presented claim is apparent from the specification as filed, in particular, pages 24 and 25 and pages 29 and 30.

It is further to be noted that during the prosecution of Applicants' parent applications, certain references were cited. Attached hereto are completed forms PTO-1449 listing these references. Copies of the references are not provided in view of the fact that they will be readily available to the Examiner through the files of the parent applications. The Examiner is respectfully requested to take these references into account in the examination of the present application and initial them on the PTO-1449 forms.

It is believed that the application is in condition for examination and such examination is requested.

Respectfully submitted,

Eric COSSEMENT et al.

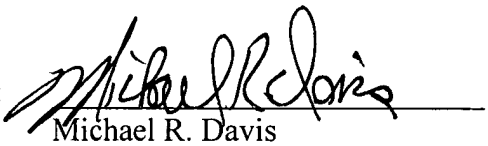
By: 

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TABLE III

Compound	pKi
C	6.2 ± 0.1
D	7.2 ± 0.2
E	5.9 ± 0.2
F	6.2 ± 0.0
G	7.6 ± 0.1
H	8.7 ± 0.0
I	7.1 ± 0.0
J	8.6 ± 0.0
K	8.6 ± 0.1
L	6.8 ± 0.1
M	~~7.1 ± 0.1~~ 8.5 ± 0.1
N	~~8.5 ± 0.1~~ 7.1 ± 0.1
O	7.4 ± 0.0
P	8.2 ± 0.0

From this Table, it can be seen that the compounds of formula V have good antihistaminic activity. These results also show that there is a difference, between the pK_i values for the two enantiomers of one compound, which corresponds to a difference in relative affinity (thus in K_i) of a factor of between about 2 and 64 towards the rat cortex H_1 receptor. Such a difference indicates that the enantiomer, which has the greatest affinity for this type of receptor (for example compound J compared with the other enantiomer I), is to be used specifically as an anxiolytic or tranquilizing agent for the treatment of diseases which are caused by an excitation of the central nervous system.

2. Peripheral antihistaminic properties.

The peripheral antihistaminic properties of the compounds are determined by measuring the inhibition of the contraction of the isolated guinea pig trachea, caused by histamine, using the method described by M. H. AMIRI and G.GABELLA (Anat. Embryol., 178 (1988), 389-397).

Tracheas of Dunkin-Hartley guinea pigs of both sexes (weight: 250 - 500 g) are excised and cut into four fragments of three segments of cartilage each. These fragments are immersed in a Krebs-Heinseleit solution at 37°C containing 10^{-7} mole/l of atropine and 10^{-5} mole/l of indomethacin and are stretched with a weight of 1 g. The solution is aerated with a current of